Flame Retardant Alternatives

Proprietary C: Chloroalkyl phosphate (2)

Hazard Review

Proprietary C: Chloroalkyl phosphate (2)
Existing Data Summary Table – Human Health Endpoints

✓= Endpoint characterized by existing data * = Data available but not adequate ✘ = Endpoint not applicable

As noted in this key, a check mark indicates that an endpoint was adequately characterized by existing studies. It does not indicate a positive or negative result for that particular endpoint.

Acute Toxicity	
Oral	✓
Dermal	✓
Inhalation	*
Eye irritation	✓
Dermal irritation	✓
Skin sensitization	✓
Subchronic Toxicity	
28-Day oral	✓
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	*
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	*
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	✓
Gene mutation in vivo	✓
Chromosomal aberrations in vitro	✓
Chromosomal aberrations in vivo	✓
DNA damage and repair	
Other	

Proprietary C: Chloroalkyl phosphate (2)
Existing Data Summary Table – Properties, Fate, and Ecotoxicity

✓= Endpoint characterized by existing data * = Data available but not adequate ✘ = Endpoint not applicable

As noted in this key, a check mark indicates that an endpoint was adequately characterized by existing studies. It does not indicate a positive or negative result for that particular endpoint.

P/Chem Properties	
Water solubility	✓
Octanol/water partition coefficient	✓
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explosivity	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	✓
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	✓
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	✓
Daphnia acute EC50	✓
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	✓
Fish chronic NOAEC, LOAEC	
Daphnia chronic NOAEC, LOAEC	✓
Mysid shrimp chronic NOAEC, LOAEC	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Proprietary C: Chloroalkyl phosphate (2)
Synonym
CAS
MF
MW
SMILES

Test materials used in health effects studies included two formulations, [Formulation 1] and [Formulation 2]. Analysis of [Formulation 1] indicated an approximate ~85% content of Proprietary C, 6.7% [Chemical 1], and 5-10% related compounds. The following table shows a comparison of properties and of impurities in [Formulation 1] and a sample of [Formulation 2] (Ref. 11). [Chemical 2] was an additive to prevent scorching during foam preparation; it is a neuroleptic agent. Results for [Formulation 2]and [Formulation 3] are provided as supplemental information only, as current products do not contain [Chemical 2].

A Comparison of [Formulation 1] with [Formulation 2] (Ref. 11)		
	[Formulation 1]	**[Formulation 2]**
Acidity (mg KOH/g)	0.1-1.0	1.6
Color (APHA)	100-200	500+
Viscosity (corrected to 25°C)	2,000-3,500 cp	3,950
[Chemical Group 1]	100-500 ppm	less than detectable
[Chemical 1] (%)	4-9%	9.0%
[Chemical 2]	absent	1.5-2.0%

Human Health Endpoints

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401)

Conclusion:

The available acute oral toxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

Acute oral toxicity studies on undiluted [Formulation 1] (~85% Proprietary C) conformed to OPPTS or OECD guidelines except that survivors were not necropsied. The LD50 exceeded the current limit dose of 5,000 mg/kg for acute oral toxicity.

Critical Study:

Type: Acute oral toxicity
Species, strain, sex, number: Rat, Sprague-Dawley, 5/sex/group
Doses: Two tests performed, the first at 5,000 mg/kg (sample 83341) and the second at 2,000 mg/kg (sample 83365)
Purity: ~85% Proprietary C in [Formulation 1]; also contains ~6.7% [Chemical 1] and 5-10% "related compounds"
Vehicle: None
Observation period: 14 days
Method: Rats observed for clinical signs frequently on the first day and daily for 14 days. Animals dying prematurely were given a gross necropsy examination.
Results: Rats were fasted prior to dosing. Clinical signs included decreased activity, respiratory distress, lacrimation, oral discharge, soft stool, decreased feces, and perianal discharge. There were no specific signs of cholinesterase inhibition (myosis or fasciculations). After day 2, all low-dose survivors showed no clinical signs of toxicity. Necropsy findings included effects in the gastrointestinal system (stomach containing air and reddish-yellow material, small intestine containing mucoid material, injected blood vessels of stomach and small intestines), kidney (dark coloration and congestion), thymus (dark coloration and mottling), lungs (redness), lymph nodes (darkened), and liver (pale). Mortality, all within 48 hours of dosing, was 1/10 at the low dose and 8/10 at the high dose. Acute oral LD50 (not calculated) was between 2,000 and 5,000 mg/kg.
Comment: The doses used in this study were equivalent to limit doses under OPPT guidelines
Reference: Ref. 6

Additional information:

An acute oral toxicity study conducted by Ref. 21 that reported an LD50 of 160 mg/kg in Sprague-Dawley rats exposed to [Formulation 3] in 10% aqueous solution was not considered, since compositional data were not available. Analysis of a similar material ([Formulation 2]) indicated that the [Chemical 1] content was twice that of [Formulation 1], and also indicated the presence of 1.5-2% [Chemical 2], a neuroleptic agent that may have contributed to the higher relative toxicity compared to [Formulation 1] (Ref. 11).

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The available acute dermal toxicity data were judged adequate to meet the endpoint.

***Basis for Conclusion*:**

Despite not fully conforming to OPPTS or OECD guidelines, the available study on [Formulation 1] appears to be adequate since neither clinical signs nor mortality were observed at the limit dose of 2,000 mg/kg. A similar LD50 was reported for [Formulation 3].

Critical Study:

Type: Acute dermal toxicity
Species, strain, sex, number: Rabbit, New Zealand albino, 3/sex
Dose: 2,000 mg/kg
Purity: ~85% Proprietary C in [Formulation 1]
Vehicle: None
Exposure period: 24 hours
Method: Hair was clipped from entire trunk of each rabbit. Skin of 1 male and 2 females was left intact; skin of 2 males and 1 female was abraded. Test material applied under occlusive bandage. Animals examined for clinical signs "frequently" during first day and daily for 14 days. Test sites were washed with saline after 24 hours; irritation assessed at 26 hours, 72 hours, and 7 days. No gross necropsy was performed.
Results: No deaths occurred; therefore, the acute dermal LD50 exceeded 2,000 mg/kg in rabbits. There were no clinical signs of toxicity and no body weight effects.
Reference: Ref. 7

Additional information:

An acute dermal LD50 exceeding 5,010 mg/kg in rabbits was reported for [Formulation 3] (Ref. 21). No compositional information was available for this material, but analysis of [Formulation 2] indicated that the [Chemical 1] content was twice that of [Formulation 1], and also indicated the presence of 1.5-2% [Chemical 2], a neuroleptic agent (Ref. 11).

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300; OECD Guideline 403)

Conclusion:

The available acute inhalation toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No verifiable acute inhalation toxicity data were located, but an incomplete robust summary for a study apparently conducted under the guideline was available in an unevaluated IUCLID Dataset (Ref. 3).

According to a robust summary for a GLP-compliant study (Ref. 3), the acute (4-hour) inhalation LC50 for Proprietary C (as [Formulation 4] or [Formulation 5]) exceeded 1.65 mg/L.

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The available eye irritation data were judged adequate to meet the endpoint.

Basis for Conclusion:

An acute eye irritation study on [Formulation 1] was essentially consistent with OPPTS and OECD guidelines. The only effect was conjunctival irritation that was resolved by 24 hours.

Critical Study:

Type: Acute eye irritation
Species, strain, sex, number: Rabbit, New Zealand White, sex not reported, 6
Doses: 0.1 mL
Purity: ~85% Proprietary C in [Formulation 1]
Vehicle: None
Method: 0.1 mL of the neat test material was instilled into one eye and not washed. The eyes were scored for irritation at 1, 24, 48, and 72 hours.
Results: The average scores (maximal possible 110) were 5.0, 0, 0, and 0 at 1, 24, 48, and 72 hours, respectively, based on conjunctival effects. No irritation of the cornea or iris was observed.
Reference: Ref. 8

Additional information:

An acute eye irritation study on [Formulation 3] reported conjunctival effects persisting to 24 hours, but resolved by 42 hours (Ref. 21). Compositional information was not available for this material, but analysis of a related substance ([Formulation 2]) indicated that its greater irritation properties, relative to [Formulation 1], might be attributed to its greater acidity: titration with 1.6 mg KOH/g, compared to 0.1-1.0 mg KOH/g, respectively (Ref. 11). A submitted confidential study reported slight eye (conjunctival) irritation.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusion:

The available dermal irritation data were judged adequate to meet the endpoint.

Basis for Conclusion:

An acute (24-hour) dermal irritation study for [Formulation 1] was consistent with OPPTS and OECD guidelines. The test material was characterized as non-irritating.

Critical Study:

Type: Acute (24-hour) dermal irritation
Species, strain, sex, number: Rabbit, New Zealand White, 3/sex
Doses: 0.5 mL to each test site (abraded, non-abraded) on each animal
Purity: ~85% Proprietary C in [Formulation 1]
Vehicle: None
Method: Hair was clipped from sides and backs of 6 rabbits; on one side, skin was abraded with point of 22 gauge needle. The test material was applied occluded; after 1 hour, Elizabethan collars were used to prevent disturbance of test sites. Sites were cleaned after 24 hours. Sites were examined for irritation at 26 hours and 72 hours after application.
Results: Males showed no signs of irritation (erythema or edema). No edema was observed in females. Barely perceptible irritation (erythema) was detected in 2/3 females at 26 hours (mean scores of 0.3 on intact and 0.2 on abraded skin), but in none at 72 hours; the primary irritation index was 0.1/8.0. The study authors characterized the material as a "non irritant" to skin following occlusive exposure for 24 hours.
Reference: Ref. 9

Additional information:

A 4-hour dermal irritation study in rabbits exposed to [Formulation 3] also reported erythema but no edema, with effects resolving by 48 hours (Ref. 21). No compositional information was available for this material, but analysis of [Formulation 1] indicated that the [Chemical 1] content was twice that of [Formulation 1] and its acidity was greater: titration with 1.6 mg KOH/g, compared to 0.1-1.0 mg KOH/g, respectively (Ref. 11). Of two submitted confidential skin irritation studies, one reported slight irritation (erythema) and another reported mild irritation (erythema and edema).

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The available skin sensitization data were judged adequate to meet the endpoint.

Basis for Conclusion:

The available studies, two of which indicate no evidence of dermal sensitization and one of which indicates evidence of mild dermal sensitization, appear to have been consistent with OPPTS and OECD guidelines. Few details were available for the Buehler test on [Formulation 1] (~85% Proprietary C), but this method is one considered preferable under OPPTS guideline 870.2600. No sensitization was reported for [Formulation 2], although analyses suggest that it is less pure than [Formulation 1], having double the content of [Chemical 1] and slightly greater acidity than the latter, and containing 1.5-20% [Chemical 2] as a scorch inhibitor (Ref. 11).

Critical Studies:

Type: Dermal sensitization (Buehler) study
Species, strain, sex, number: Guinea pig, Hartley albino, 5/sex/group
Doses: Not reported, but probably 0.5 mL, since Buehler method is cited.
Purity: ~85% Proprietary C in [Formulation 1]
Vehicle: None
Method: Cited as Ritz and Buehler. The test material was applied dermally once per week for 3 weeks. Fourteen and 21 days after the third application, challenge and rechallenge doses were applied to treated animals and to a set of previously untreated controls (5/sex). Skin responses were evaluated at 24 and 48 hours after the initial challenge and rechallenge.
Result: No sensitization reactions were observed.
Reference: Ref. 19

Type: Dermal sensitization study
Species, strain, sex, number: Guinea pig, albino, 10 males/group
Doses: 0.05 mL of 10% or 25% (v/v)
Purity: Not reported; [Formulation 2]
Vehicle: 13% guinea pig fat dissolved in 50/50 acetone/dioxane (FAD)
Method: The test material was applied to shaved intact shoulder skin and gently rubbed in with a Teflon rod. Sensitization by 4 sacral intradermal injections of 0.1 mL of 1% solution in DMSO. Challenge after 2 weeks by 0.05 mL of 10 or 25% (v/v) in FAD applied to shaved intact shoulder skin. Groups of previously exposed animals (10/dose) were also given the challenge doses.
Result: Reactions after 1 day were negative for all groups. The authors conclude that the material is not a dermal sensitizer.
Reference: Ref. 4

Additional information:

One-inch squares of acetate fiber with 5.0% [Formulation 2] did not elicit skin reactions when applied for 6 days to the skin of 211 human subjects (Ref. 4). Two weeks later, no sensitization reactions were observed following a 48-hour challenge application. A confidential sensitization study reported mild skin sensitization in a guinea pig maximization test, with 17% of the animals showing positive results.

SUBCHRONIC TOXICITY

Conclusion:

The available subchronic toxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

A submitted confidential 28-day or gavage study was consistent with guidelines.

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

- **Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)**

A confidential, 4-week, repeated-dose oral gavage study in rats was submitted. The NOAEL and LOAEL were 15 and 150 mg/kg/day, respectively, based on liver effects

No pertinent studies were located that addressed the subchronic toxicity endpoints in the guidelines listed below.

- **90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)**

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

Subchronic Dermal Toxicity (21/28-day or 90-day)
- 21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)
- 90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)

Subchronic Inhalation Toxicity (90-day)
- 90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3465; OECD Guideline 413)

REPRODUCTIVE TOXICITY

Conclusion:

No available reproductive toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the reproductive toxicity endpoints in the guidelines listed below.

Additional Information

A confidential, 4-week repeated-dose oral gavage study in rats was submitted. No histopathology was found in the reproductive organs in either sex at a NOAEL of 600 mg/kg/day; however, the study duration was relatively short and reproductive function was not tested.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)**

DEVELOPMENTAL TOXICITY

Conclusion:

The available developmental toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

Although [Formulation 2] apparently has a similar if lower Proprietary C content compared to [Formulation 1] (~85% Proprietary C), it also contains 1.5-2.0% [Chemical 2] as an anti-scorching additive (Ref. 11). The presence of [Chemical 2], a neuroleptic, could confound the identification of the maternal NOAEL/LOAEL values. The small group size prevents the identification of fetal NOAEL/LOAEL values.

Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)

Type: Prenatal developmental toxicity
Species, strain, sex, number: Rat, CD, 5 pregnant females/group
Purity: Not reported; [Formulation 2]
Doses: 0 (distilled water at volume of high-dose), 100, 200, 400, 800, and 1,600 mg/kg/day
Vehicle: none
Exposure duration, frequency: gestational days (GD) 6-19
Method: Pregnant rats were treated once daily on GD 6-17 by oral gavage and were observed once daily on GD 6-20 for mortality and clinical signs. Maternal body weights were measured on GD 0, 6, 9, 12, 16, and 20. Dams dying prematurely were necropsied to determine cause of death. Examinations of thoracic and abdominal cavities for gross lesions, ovaries, and uterine contents were conducted on all surviving dams on GD 20. Endpoints included fetal viability, early and late resorptions, post- implantation loss, total implantations, and corpora lutea.
Results: Maternal mortality was observed in 5/5 at 1,600 mg/kg/day (GD 7 and 8) and 1/5 at 800 mg/kg/day (GD 9); causes of death were not determined. Treatment-related clinical signs were not observed at $\leq$200 mg/kg/day. Clinical signs included dry red matter around the nose and forepaws (in 1 rat at 400 mg/kg/day and 2 rats at 800 mg/kg/day), and staining of the anogenital area (in 4/5 rats at 800 mg/kg/day). Maternal body weight gain was reduced by 32% at 800 mg/kg/day (largely because of weight loss during GD6-9), but not affected at lower doses. A slight increase in mean postimplantation losses (1.0 per dam) at 800 mg/kg/day (compared to 0.6 per dam in concurrent

controls) was similar to the mean historical control value of 0.9 per dam. No other significant treatment-related effects were observed. The maternal NOAEL was 400 mg/kg/day and the LOAEL was 800 mg/kg/day for clinical signs (anogenital staining) and increased mortality (1/5). [Formulation 2] was not a specific developmental toxicant as the only effect in offspring (marginally increased postimplantation loss) occurred at a maternally toxic dose (800 mg/kg/day). The small group size (four surviving dams) does not permit accurate identification of fetal NOAEL/LOAEL values.
Reference: Ref. 5

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**

No studies were located that followed or were similar to the two tests listed above.

CHRONIC TOXICITY

Conclusion:

No available chronic toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the chronic toxicity endpoints in the guidelines listed below.

- **Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

CARCINOGENICITY

Conclusion:

No available carcinogenicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the carcinogenicity endpoints in the guidelines listed below.

- **Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)**

- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

NEUROTOXICITY

Conclusion:

The available neurotoxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No neurotoxicity studies were available that followed guideline methods. However, inhibition of cholinesterase activity, an optional parameter for delayed neurotoxicity in hens under OPPTS Guideline 870.6100, was noted in rats orally exposed to [Formulation 1] (~85% Proprietary C) (Ref. 10, 14).

No studies were located that followed or were similar to the guidelines listed below.

- **Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)**
- **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**
- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**
- **Additional neurotoxicity studies:**
    - Schedule-Controlled Operant Behavior (mouse or rat) (OPPTS Harmonized Guideline 870.6500)
    - Peripheral Nerve Function (rodent) (OPPTS Harmonized Guideline 870.6850)
    - Sensory Evoked Potentials (rat, pigmented strain preferred) (OPPTS Harmonized Guideline 870.6855)

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Additional Neurotoxicity Studies:

A submitted confidential, 4-week repeated-dose oral gavage study in rats included a neurotoxicity screening battery. No behavioral effects or neurohistopathology were found at a NOAEL of 600 mg/kg/day.

Cholineserase Inhibition

Depression of serum cholinesterase activity was observed in male and female Sprague-Dawley rats given 500 or 1,500 mg/kg [Formulation 1] (~85% Proprietary C) by gavage (Ref. 10); females were

more sensitive than males. Suppression was by ~33% in males and ~78% in females after 1 hour and was maximal at 8 hours by ~62% in males and ~93% in females.

In a study comparing three different [Formulation 1] samples (from two different manufacturing protocols), female Sprague-Dawley rats (4/group) were treated with 0 or 250 mg/kg by oral gavage in 50% aqueous polyethylene glycol 200 (Ref. 14). Four hours later, serum cholinesterase activity was suppressed by 60-70% for [Sample 1] and [Sample 2] and by ~30% for [Sample 3].

Groups of four female Sprague-Dawley rats were administered [Formulation 1] at 0, 15, 50, 150, 500, or 1,500 mg/kg by oral gavage in 50% aqueous polyethylene glycol 200 (Ref. 12). After 4 hours, depression of serum cholinesterase activity was statistically significant and dose-related, compared to controls in groups treated at ≥50 mg/kg. In this study, brain cholinesterase levels were not significantly affected four hours after treatment at doses as high as 1,500 mg/kg.

Groups of three female New Zealand white rabbits were untreated (controls) or dermally administered 2,000 mg/kg [Formulation 1] (Ref. 13). Dermal treatment caused no significant suppression of cholinesterase activity measured in serum and whole blood at 7 or 24 hours or in brain at 24 hours.

IMMUNOTOXICITY

***Conclusion*:**

No available immunotoxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the endpoints in the guidelines listed below.

- **Immunotoxicity (OPPTS Harmonized Guideline 870.7800)**

GENOTOXICITY

Conclusion:

The available genotoxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

Mutagenicity testing of [Formulation 1] (~85% Proprietary C) in mammalian cells *in vitro* was conducted under methods equivalent to OPPTS and OECD guidelines. The chromosomal aberration endpoint for Proprietary C is satisfied by adequate submitted confidential studies: a chromosomal aberrations assay in human lymphocytes *in vitro* and an *in vivo* micronucleus assay in mice.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

No verifiable studies were located for bacterial mutagenicity assays following or similar to the guideline listed above, but a robust summary for a GLP-compliant study was included in an unevaluated IUCLID Dataset (Ref. 3).

As described in an incomplete robust summary Ref. 2 conducted a mutagenicity (Ames) assay in *Salmonella typhimurium* strains TA98 and TA100 for Proprietary C (Formulation 4 or Formulation 5) (Ref. 3). Results were negative with or without metabolic activation at concentrations as high as 5 mg/plate. This study would not completely satisfy the guideline, since only two strains were tested.

- **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

Critical Study:

Type: Mammalian Cell Gene Mutation Test: Forward Mutation
Species, strain: Mouse lymphoma L5178Y
Metabolic activation: Tested with and without Aroclor-1242-induced liver S9 from Sprague-Dawley rat
Concentrations: 0.01-0.8 µL/mL without S9 and 0.06-0.15 µL/mL with S9
Purity: ~85% Proprietary C as [Formulation 1]; also contains 6.7% [Chemical 1], and 5-10% related compounds
Method: Selection of forward mutation from $TK^{+/-}$ to $TK^{-/-}$ genotype. Activity compared to positive controls (ethylmethylsulfonate and dimethylbenzanthracene) and vehicle (DMSO).
Results: No increase in forward mutations was observed.
Reference: Ref. 15

Additional information:

Similar mouse lymphoma mutagenicity assays conducted on [Formulation 1] containing 0.05-0.25% [Chemical 3] also yielded negative results (Ref. 16, 17, 18).

Chromosomal Aberration in Vitro:

- **In Vitro Mammalian Chromosome Aberration Test (OPPTS Harmonized Guideline 870.5375)**

A submitted confidential study reported negative results for chromosomal aberrations in cultured human lymphocytes.

Chromosomal Aberrations in Vivo:

- **Mammalian erythrocyte micronucleus test (OPPTS Harmonized Guideline 870.5395)**

A submitted confidential study reported negative results for micronucleus formation in bone marrow of mice exposed by oral gavage.

No genotoxicity studies relevant to the following categories or to other types of genotoxic effects were submitted.

Gene Mutation in Vivo
DNA Damage and Repair

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

- The currently available data were judged adequate to meet the endpoints for acute freshwater toxicity to fish, aquatic invertebrates, and algae.

- The existing data for acute marine/estuary toxicity for fish, aquatic invertebrates, and algae were judged inadequate to meet these endpoints.

Basis for Conclusion:

A study exists of the acute toxicity to mysid shrimp of wastewater generated during the manufacture of the flame-retardant compound [Formulation 1] (Ref. 20). A handwritten correction on the title page of the study indicates that the wastewater samples were from the production of [Formulation 1], not [Formulation 4]. [Formulation 1] contains Proprietary C; however, the wastewater samples used in the study contained a mixture of compounds, none of which appeared to be Proprietary C.

No pertinent acute toxicity studies with fish, aquatic invertebrates, or algae were located that addressed the endpoints in the guidelines listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**

A confidential study with a 96-hour LC50 of 52.2 mg/L in freshwater fish was submitted. These data were judged adequate to meet the endpoint.

- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**

A confidential study with a 48-hour EC50 of 41.9 mg/L in freshwater invertebrates was submitted. These data were judged adequate to meet the endpoint.

- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**

A study exists of the acute toxicity to mysid shrimp of wastewater generated during the manufacture of the flame-retardant compound [Formulation 1] (Ref. 20). A handwritten correction on the title page of the study indicates that the wastewater samples were from the production of [Formulation 1], not [Formulation 4]. [Formulation 1] contains Proprietary C; however, the wastewater samples used in the study contained a mixture of compounds, none of which appeared to be Proprietary C.

- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

A confidential study with 96-hour EC50 values for freshwater algal growth inhibition and growth rate inhibition of 20.1 and 38.5 mg/L, respectively, was submitted. These data were judged adequate to meet the endpoint.

Chronic Toxicity to Aquatic Organisms

Conclusion:

No available chronic toxicity data for fish and aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates were located that addressed the endpoints in the guidelines listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**

- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**

A confidential chronic toxicity to freshwater invertebrates study was submitted. The 23-day EC50 for parental mortality was 7.31 mg/L. The NOEC and LOEC for impaired reproduction were ≥3.68 mg/L and >3.68 mg/L, respectively. These data were judged adequate to meet the endpoint.

- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

No relevant data were located for chronic toxicity to marine/estuarine invertebrates.

Acute and Subchronic Toxicity to Terrestrial Organisms

Conclusion:

No available acute and subchronic toxicity data for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, acute dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms were located that addressed the endpoints in the guidelines listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**
- **Acute Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

Physical/Chemical Properties

Proprietary C
CAS
MF
MW
SMILES

Water Solubility (mg/L):

Conclusion:

The available water solubility data are adequate.

Basis for Conclusion:

A confidential experimental study for the water solubility of Proprietary C was submitted. Using OECD Guideline 105, a water solubility of 232 mg/L at 20°C was measured.

Log K_{ow}:

Conclusion:

The available log K_{ow} data are adequate.

Basis for Conclusion:

A confidential experimental study for the log K_{ow} of Proprietary C was submitted. Using OECD Guideline 107, a log K_{ow} of 2.83 was measured using the shake flask method.

Oxidation/Reduction: No data

Melting Point: No data

Vapor Pressure (torr): No data

Odor: No data

Oxidation/Reduction Chemical Incompatibility: No data

Flammability: No data

Explosivity: No data

Corrosion Characteristics: No data

pH: No data

UV/VIS Absorption: No data

Viscosity: No data

Density/Relative Density/Bulk Density: No data

Dissociation Constant in Water: No data

Henry's Law Constant: No data

Environmental Fate

Bioconcentration

Fish: No data

Daphnids: No data

Green Algae: No data

Oysters: No data

Earthworms: No data

Fish Metabolism: No data

Degradation

Photolysis in the Atmosphere: No data

Photolysis in Water: No data

Photolysis in Soil: No data

Aerobic Biodegradation: Confidential experimental studies on the biodegradation of Proprietary C indicate 37% oxygen uptake after 28 days in OECD 302C, 5% degradation in modified Sturm test over 28 days, and 8-15% inhibition to activated sludge.

Anaerobic Biodegradation: No data

Porous Pot Test: No data

Pyrolysis: No data

Hydrolysis as a Function of pH:

Conclusion:

The available hydrolysis data are adequate.

Basis for Conclusion:

A confidential experimental study on the hydrolysis of Proprietary C was submitted. Conducted according to EEC guideline C.7, the hydrolytic stability of Proprietary C at pH 4, 7, and 9 was

determined at 50°C and it was found to undergo <10% degradation after 5 days. The hydrolysis half-life at 25°C was determined to be greater than 1 year.

Sediment/Water Biodegradation: No data

Soil Biodegradation with Product Identification: No data

Indirect Photolysis in Water: No data

Sediment/Soil Adsorption/Desorption: No data